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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,928	MERCKEN ET AL.	
	Examiner	Art Unit	
	CHANG-YU WANG	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-25, 28 and 31-36* is/are rejected.

7)☒ Claim(s) *26,27,29 and 30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/26/09 has been entered.

Status of Application/Amendments/claims

2. Applicant's amendment filed 8/26/09 is acknowledged. Claims 1-16 are cancelled. Note that there is a duplicate of claim 34 recited on p. 3 of the claim set. The second claim 34 and claim 35 are renumbered as claims 35 and 36 respectively. Claims 17-36 are newly added. Claims 17-36 are pending in this application and under examination in this office action.

3. Any objection or rejection of record, which is not expressly repeated in this office action, has been overcome by Applicant's response.

4. Applicant's arguments filed on 8/26/09 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Withdrawn

5. The rejection of claims 14 and 16 under 35 U.S.C. 112, first paragraph, because the specification does not enable the invention commensurate in scope with the claims is moot because the claims are canceled.

The rejection of claims 2, 6, 7, 15 and 16 under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent No. 6984720 (Korman et al. issued on Jan 10, 2006, priority Aug 24, 1999) is withdrawn in response to Applicant's arguments on p.11-12 of the response and cancellation of the claims.

The rejection of claims 2-11 and 14-16 under 35 U.S.C. 103(a) as being unpatentable over Huse et al. (Huse et al. J. Biol. Chem. 2002. 277: 16278-16284) in view of Walker et al (J. Neuropathol. Exp. Neurol.1994 Jul. 53: 377-383 as cited in the previous office action) and WO0162801 (as in IDS submitted on Mar 23, 2005 and cited in the previous office action) and further in view of US Patent No. 6984720 (Korman et al. issued on Jan 10, 2006, priority Aug 24, 1999) is withdrawn in response to Applicant's arguments on p.11-12 of the response and cancellation of the claims.

Claim Rejections/Objections Maintained

In view of the amendment filed on 8/26/09, the following rejections are maintained.

Claim Rejections/Objections

6. Claims 34 and 35 are objected to because the claim numbers are incorrect. There is a duplicate of claim 34 recited on p. 3 of the claim set. The second claim 34 and claim 35 are renumbered as claims 35 and 36 respectively.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-19, 22-23, 28 and 36 (original claim 35) are rejected under 35 U.S.C. 102 (b) as being anticipated by Walker et al (J. Neuropathol. Exp. Neurol.1994 Jul. 53: 377-383), Pirttila et al. (J. Neurol Sci. 1994 Dec 1; 127:90-5), WO0162801 (as in IDS submitted on Mar 23, 2005) or Naslund et al (as in IDS submitted on Mar 23, 2005). Claims 17-19, 22-23, 28 and 36 (original claim 35) are rejected under 35 U.S.C. 102 (b) as being anticipated by Solomon et al. (Proc. Natl. Acad. Sci. USA. 1996. 93: 452-455). Claims 17-19, 22-23, 28 and 36 (original claim 35) are rejected under 35 U.S.C. 102 (a) as being anticipated by Huse et al. (Huse et al. J. Biol. Chem. 2002. 277: 16278-16284). These rejections are maintained for the reasons made of record.

Claims 17-19, 22-23, 28 and 36 (original claim 35) as amended are drawn to a monoclonal antibody which specifically binds to a Aβ11-x polypeptide at one or more

epitopes present on the first 5-7 N-terminal amino acids, wherein the antibody does not specifically bind to a full length Aβ1-40/42 peptide and a hybridoma of the claimed antibody.

On p. 6-9 of the response, Applicant argues that none of the cited references dislcose an antibody that binds to one or more epitopes on the first 5-7 N-terminal amino acids of Aβ11-x, binds specifically to Aβ11-x and do not specifically bind to a full length Aβ1-40/42 peptides as presently claimed. Applicant's arguments have been fully considered but they are not persuasive.

In response, as previously made of record, the art antibodies were raised against Aβ1-16 (10D5 & 6E10, Walker and Naslund), Aβ17-24 (4G8, Prittila), and Aβ13-28 (266, WO01/62801) immungens and thus can bind to the epitopes of Aβ11-x including the epitopes on the first 5-7 amino acids as evidenced by Huse et al (Huse et al. J. Biol. Chem. 2002. 277: 16278-16284, cited in the previuos office action). In addition, the antibodies raised against Aβ 1-28 and 8-17 taught by Solomon et al. would inherently recognize Aβ11-x because the amino acid sequence of the immunogens (5-7 amino acids of Aβ11-x) for the instant antibodies are encompassed within the sequences of amino acids 1-28 and 8-17 of Aβ. For the same reason, the antibody BNT77 taught by Huse et al. was raised against amino acids 11-16 of Aβ, thus it can recognize N-terminal truncated species of Aβ including Aβ11-15 amd Aβ11-17 that are used to raise the claimed antibody. If the epitopes to which Applicant's antibody binds is present in

Aβ11-x, so that Applicant's antibody binds to Aβ11-x, these epitopes are also present in Aβ11-16, 1-28 and 8-17.

With regard to whether the art antibodies have the same property as the claimed antibodies that bind to Aβ11-x without specifically binding to the full length of Aβ1-40/42, it is noted that Applicant claims a product in terms of a function, property or characteristics is the same as the prior art products. Note that

"Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.' In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." See MPEP § 2112.01 [R-3].

As previuosly made of record, if the epitopes which Applicant's antibody binds to are present in Aβ11-x, so that Applicant's antibody binds to Aβ11-x, these epitopes are also present in Aβ 1-16, 17-24, and 13-28.

It is known in the art that anti-Aβ antibodies can cross react with different species or different lengths of Aβ peptides in different titrations because of their different binding affinity. Applicant has provided no showing that the antibodies in the art have characteristics different from those specified by Applicant and do not cross react with the full length of Aβ1-40/42 under the same titration or concentration and under the same incubation conditions as those of the prior art. Applicant fails to provide side-by-side comparisons to demonstrate that the claimed antibody is different from those antibodies disclosed by Walker et al., Pirtila, WO0162801, Naslund and Huse.

Since the claimed antibody is substantially identical to the art antibodies in structure or composition and is able to bind to Aβ11-x, the antibodies disclosed by Walker et al., Pirtila, WO0162801, Naslund and Huse farily anticipate the claimed antibody because Applicant fails to demonstrate that the claimed antibody has a function, property or characteristics different from the antibodies dislcosed by the art.

Accordingly, the rejection of claims 17-19, 22-23, 28 and 36 (original claim 35) under 35 U.S.C. 102 (b) as being anticipated by Walker et al., Pirttila et al., WO0162801 or Naslund et al. is maintained. The rejection of claims 17-19, 22-23, 28 and 36 (original claim 35) under 35 U.S.C. 102 (b) as being anticipated by Solomon et al. or by Huse et al. is maintained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 17-25, 28 and 31-36 (original claim 35) are rejected under 35 U.S.C. 103(a) for being unpatentable over Huse et al. (Huse et al. J. Biol. Chem. 2002. 277: 16278-16284) in view of Walker et al (J. Neuropathol. Exp. Neurol.1994 Jul. 53: 377-383) and WO0162801. The rejection is maintained for the reasons made of record.

Claims 17-25, 28 and 31-36 (original claim 35) as amended are drawn to a monoclonal antibody which specifically binds to a Aβ11-x polypeptide at one or more epitopes present on the first 5-7 N-terminal amino acids, wherein the antibody does not specifically bind to a full length Aβ1-40/42 peptide, a hybridoma of the claimed antibody and methods of detecting Aβ11-x peptide in a sample or diagnose AD by detecting and comparing the amount of Aβ11-x in a test sample and a control.

On p. 9-10 of the response, Applicant argues that all of the antibodies disclosed by Huse lack one or more properties of the claimed antibodies. Applicant argues that none of the art provides motivation to modify the antibodies of Huse to arrive at the claimed antibodies. Applicant argues that Huse teaches away from the claimed invention because Huse teaches an antibody produced with the first 5 N-terminal amino acids of Aβ11-x (i.e. Aβ11-16 immunogen) would also bind to the full length Aβ1-40/42. Applicant aruges that both Walker and WO0162801 are silent as to whether the disclosed antibodes bind to Aβ11-x and thus cannot cure the deficiency in Huse. Applicant's arguments have been fully considered but they are not persuasive.

In response, for the reasons set forth above in section of the 102 rejection at paragraph 7, the antibodies disclosed by Huse et al., Walker et al. and WO0162801 do

recognize Aβ11-x because the antibodies disclosed by Huse et al., Walker et al. and WO0162801 have been shown to have the same property as the claimed antibodies.

In addition, the examiner asserts that Huse does not teach away from the claimed invention because the antibody disclosed by Huse was raised against Aβ11-16, which meets the limitation of the claim 17.

Furthermore, WO0162801 teaches hybridoma, humanized and chimeric antibodies and a diagnostic composition comprising the claimed antibodies as in claims 24-25, 28 and 36 (original claim 35). WO0162801 also teaches a method of detection of Aβ in the brain tissue and CSF of Alzheimer's disease patients using labeled antibodies by electrophoresis or ELISA as recited in instant claims 20-21 and 31-35 (including duplicate claim 34) (see p.26, examples 1-2; p. 30, example 6, in particular). Thus, It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to use the antibody raised against Aβ11-16 or use the antibody that can recognize Aβ11-x to detect Aβ11-x in Alzheimer's disease because the level of Aβ11-40/42 has been shown increased in AD patients. The person of ordinary skill in the art would have been motivated do so with an expectation of success in using an antibody that recognize Aβ11-x to detect diseases associated Aβ formation because the antibody against Aβ11-16 is able to detect Aβ11-40/42 in AD brains.

Note that only a reason, suggestion or motivation need appear in the cited prior art in order to combine references under 35 U.S.C. 103. *Pro Mold Tool Col. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. MPEP. §2144.07.

New Grounds of Rejection Necessitated by the Amendment

The following rejections are new grounds of rejections necessitated by the amendment filed on 8/26/09.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required

feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 18 and 19 recite the broad recitation “binds to human Abeta11-x" and "binds to mouse Abeta11-x" respectively, and the claims also recite “specifically binds to a Abeta11-x polypeptide at one or more epitopes present on the first 5 to 7 N-terminal amino acids", which is the narrower statement of the range/limitation. Thus the claims are indefinite.

Conclusion

Allowable Subject Matter

10. Claims 26-27, 29 and 30 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. Claims 17-25, 28 and 31-36 (original claim 35) are rejected.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-

4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chang-Yu Wang, Ph.D.
October 15, 2009

/Chang-Yu Wang/
Examiner, Art Unit 1649